PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis*.3(c) and 72.2)

To:

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Eingegangen
Gulde Hengelhaupt Ziebig & Schneider
26. JULI 2006

Date of mailing *(day/month/year)* 20 July 2006 (20.07.2006)	
Applicant's or agent's file reference P201703PC-L	WV IMPORTANT NOTIFICATION
International application No. PCT/DE2004/001897	Frist International filing date *(day/month/year)* 26 August 2004 (26.08.2004)
Applicant BRD, VERTRETEN DURCH DAS BUNDESMINISTERIUM FÜR GESUNDHEIT UND SOZIALE SICHERUNG, LETZTVERTRETEN DURCH DEN PRÄSIDENTEN DES ROBERT-KOCH-INSTITUTES et al	

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Agnes Wittmann-Regis
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Form PCT/IB/338 (January 2004)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference P201703PC-L	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/DE2004/001897	International filing date *(day/month/year)* 26 August 2004 (26.08.2004)	Priority date *(day/month/year)* 26 August 2003 (26.08.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant BRD, VERTRETEN DURCH DAS BUNDESMINISTERIUM FÜR GESUNDHEIT UND SOZIALE SICHERUNG, LETZTVERTRETEN DURCH DEN PRÄSIDENTEN DES ROBERT-KOCH-INSTITUTES		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 13 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 10 July 2006 (10.07.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Agnes Wittmann-Regis e-mail: pt06@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

Translation

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference P201703PC-L	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DE2004/001897	26.08.2004	26.08.2003

International Patent Classification (IPC) or both national classification and IPC

Applicant

BRD, VERTRETEN DURCH DAS BUNDESMINISTERIUM FÜR GESUNDHEIT UND SOZIALE SICHERUNG, LETZTVERTRETEN DURCH DEN PRÄSIDENTEN DES

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. I **Basis of this opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☒ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

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Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 1-32 (in part) and additionally 21-30(with respect to IA)

because:

☒ the said international application, or the said claims Nos. 21-30 (with respect to IA)
relate to the following subject matter which does not require an international preliminary examination (*specify*):

See supplemental sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-32 (in part)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/DE2004/001897

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

See supplemental sheet

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-32 (in part)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/DE2004/001897

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		YES
	Claims	1-32	NO
Inventive step (IS)	Claims		YES
	Claims	1-32	NO
Industrial applicability (IA)	Claims	1-20,31,32	YES
	Claims		NO

2. Citations and explanations:

Reference is made to the following documents:

D1: WO 02/079239 A (U.S. ARMY MEDICAL RESEARCH INSTITUTE OF INFECTIOUS DISEASES; GROGAN) 10 October 2002 (2002-10-10)

D2: WO 01/16183 A (U.S. ARMY MEDICAL RESEARCH INSTITUTE OF INFECTIOUS DISEASES; HART, MAR) 8 March 2001 (2001-03-08)

D3: FR-A-2 586 427 (PASTEUR INSTITUT) 27 February 1987 (1987-02-27)

D4: EP-A-0 331 961 (ABBOTT LABORATORIES) 13 September 1989 (1989-09-13)

D5: WO 98/20036 A (GENENTECH, INC) 14 May 1998 (1998-05-14)

D6: DATABASE EBI [Online] 1 September 1990 (1990-09-01), found in EBI accession no. P16899

D7: DE 199 57 838 A1 (HEINRICH-PETTE-INSTITUT) 13 June 2001 (2001-06-13)

D8: FR-A-2 832 424 (GENETHON III) 23 May 2003 (2003-05-23)

D9: FIEBIG U ET AL: "Neutralizing antibodies against conserved domains of p15E of porcine endogenous retroviruses: Basis for a vaccine for

xenotransplantation?" VIROLOGY, RAVEN PRESS, NEW YORK, NY, US, vol. 307, no. 2, 15 March 2003 (2003-03-15), pages 406-413, XP002269727 ISSN: 0042-6822

D10: DATABASE EMBL [Online] 1 May 2000 (2000-05-01), found in EBI Database accession no. Q9TTC0

D11: DATABASE EBI [Online] 13 August 1987 (1987-08-13), Database accession no. P04502

Novelty

The present application does not meet the requirements of PCT Article 33(1) because the subject matter of independent claims 1,9,17-19,21,25,26,29,31 and 32 is not novel under PCT Article 33(2).

It should be noted that the complete GP2, gp41 and p15E proteins are in each case considered immunogenic constructs in accordance with claim 1 because said proteins comprise in their entire length both the first and the second region according to claim 1(i) and 1(ii).

Document D1 discloses (the references between parentheses refer to this document) an immunogenic construct which includes the Ebola GP2 domain and which comprises both the first region of GP2, located between the transmembrane passage and a first alpha-helical structure, and the second region located between the fusion domain and a second alpha-helical structure.
D1 further discloses an amino acid sequence which is 100% homologous to SEQ ID NO: 69 and almost 100% homologous to

SEQ ID NO: 68 of the present application.
Immunogenic constructs of this kind may be employed in the treatment of Ebola and may serve as vaccines or to detect the viruses (see pages 5 to 9; claims 1 to 48; examples 2 to 5; sequences 12 and 13).

Document D2 discloses (the references between parentheses refer to this document) antibodies to Ebola GP. D2 also discloses a sequence which includes the Ebola GP2 domain and which comprises both the first region of GP2, located between the transmembrane passage and a first alpha-helical structure, and the second region located between the fusion domain and a second alpha-helical structure. This amino acid sequence is 100% homologous to SEQ ID NO: 69 and almost 100% homologous to SEQ ID NO: 68 of the present application.
Immunogenic constructs of this kind may be employed in the treatment of Ebola and may serve as vaccines or to detect the viruses (see SEQ ID NO: 2 and claims).

Document D3 describes a sequence of the visna virus transmembrane envelope protein gp41, which is highly homologous to sequences 38 and 39 of the present application and which may be used for the diagnosis of visna infections (see claims 1-9).

Document D4 describes a sequence of the SIVmac transmembrane envelope protein gp41, which is highly homologous to sequence 34 of the present application (see figure 14).

Document D5 describes a sequence of the SIVcpz

transmembrane envelope protein gp41, which is highly homologous to sequence 36 of the present application (see SEQ ID NO: 106).

Document D6 describes a sequence of the OMVV transmembrane envelope protein gp41, which is highly homologous to sequences 32 and 33 of the present application (see abstract).

Document D7 discloses a gp41 fusion peptide connected C-terminally via a linker to a transmembrane anchor, which may be used for gene therapy of HIV infection (see claims 1 to 23).

Document D8 describes a sequence of the GALV transmembrane envelope protein p15E, which is highly homologous to sequences 54 and 55 of the present application (see SEQ ID NO: 3).

Document D9 describes a sequence of the PERV transmembrane envelope protein p15E, which is highly homologous to sequences 101 and 102 of the present application (see figure 3).

Document D10 describes a sequence of the KoRV transmembrane envelope protein p15E, which is highly homologous to sequences 103 and 104 of the present application (see abstract).

Document D11 describes a sequence of the MuLV transmembrane envelope protein p15E, which is highly homologous to sequences 56 and 57 of the present

application (see abstract).

Dependent claims 2-8, 10-16, 20,22-24,27,28 and 30 do not contain any features which, in combination with the features of any claim to which they refer, meet the PCT requirements for novelty and inventive step, see D1 to D11 and the corresponding passages cited in the search report.

Industrial applicability

The PCT Contracting States do not have uniform criteria for assessing the industrial applicability of claims 21 to 30 in their present form. Patentability may also depend on the wording of the claims. The EPO, for example, does not recognize the industrial applicability of claims to the medical use of a compound; it may, however, allow claims to the first medical application of a known compound or to the use of such a compound in the manufacture of a drug for a new medical application.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/DE2004/001897

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

Box III:

Given the lack of unity of invention, the search was carried out only for the inventions for which a search fee has been paid, i.e. the first, eighth and eleventh inventions, claims 1-32 (in part).

Claims 21 to 30 relate to subject matter which, in the opinion of this Authority, falls under PCT Rule 67.1(iv). Consequently, no expert opinion has been established in respect of the industrial applicability of the subject matter of said claims (PCT Article 34(4)(a)(i)).

Box IV:

This Authority has found that the international application comprises a plurality of inventions or groups of inventions which are not linked by a single general inventive concept (PCT Rule 13.1), namely:

I: claims 1-32 (in part) to the envelope protein GP2
II: claims 1-32 (in part) to the envelope protein gp20
III: claims 1-32 (in part) to the envelope protein gp21
IV: claims 1-32 (in part) to the envelope protein gp30
V: claims 1-32 (in part) to the envelope protein gp36
VI: claims 1-32 (in part) to the envelope protein gp37
VII: claims 1-32 (in part) to the envelope protein gp40
VIII: claims 1-32 (in part) to the envelope protein gp41
IX: claims 1-32 (in part) to the envelope protein gp45

Supplemental Box

X: claims 1-32 (in part) to the envelope protein gp160

XI: claims 1-32 (in part) to the envelope protein p15E

XII: claims 1-32 (in part) to the envelope protein E2

XIII: claims 1-32 (in part) to the envelope protein HA2

XIV: claims 1-32 (in part) to the envelope protein F2

The reasons are as follows:

The problem on which the present application is based is the treatment and detection of viral infections, for example HIV, Ebola or influenza viruses. The problem is solved by providing an immunogenic construct comprising amino acid sequences of a viral transmembrane envelope protein which are selected from a first region of said envelope protein, located between the transmembrane passage and a first alpha-helical structure, and a second region located between the fusion domain and a second alpha-helical structure.

The technical feature that could link the different solutions *a priori* comprises the property of being a compound which comprises a first region of said envelope protein, located between the transmembrane passage and a first alpha-helical structure, and a second region located between the fusion domain and a second alpha-helical structure.

However, such a solution has been described previously in the prior art, for example in the international patent application WO 02/079239 which discloses *inter alia* an immunogenic construct comprising the Ebola virus GP2 domain and being nearly 100% homologous to the amino acid

Supplemental Box

sequences SEQ ID NOs: 68 and 69 of the present application (see SEQ ID NO: 12 and claims).

The problem to be solved is therefore determined by providing further immunogenic constructs for the treatment and detection of viral infections.
However, since there is, between the individual constructs of the various inventions, no structural relationship which could be considered a particular technical feature under PCT Rule 13 and since no further particular technical features can be found, the present application lacks unity of invention, resulting in the 14 different inventions indicated above.